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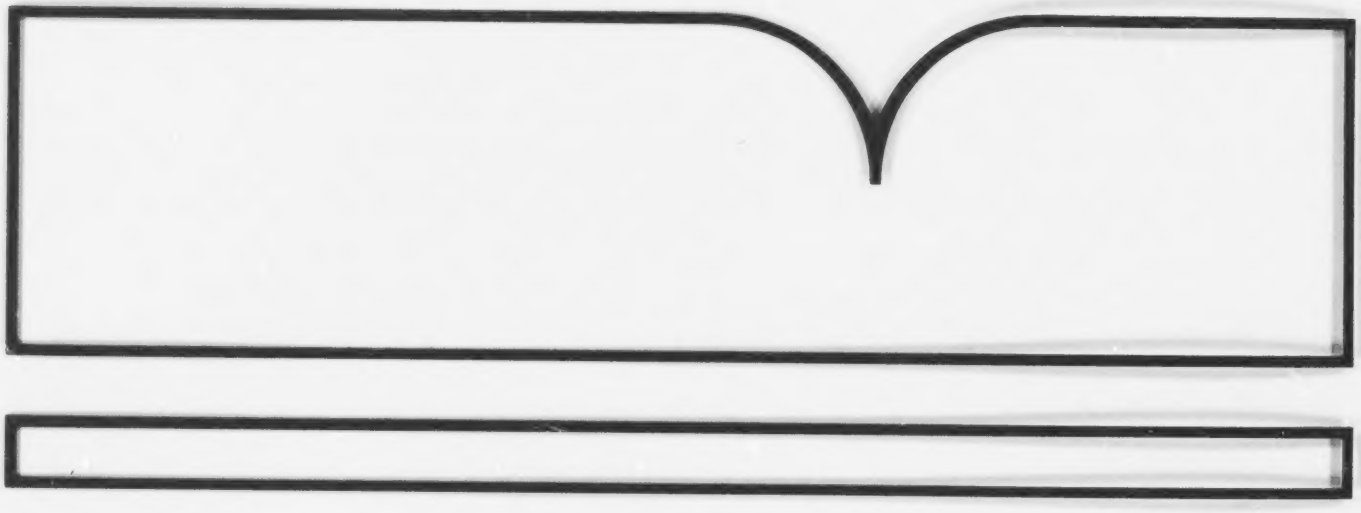

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HAZARD EVALUATION DIVISION

STANDARD EVALUATION PROCEDURE

PRODUCT CHEMISTRY

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Detailed, stepwise procedures for the evaluation of product chemistry data are provided. Topics on Product Identity and Composition (Guideline Reference Numbers 61-1,2,3), Analysis and Certification of Product Ingredients (Reference Numbers 62-1,2,3), Physical and Chemical Characteristics (Reference Numbers 63-2 thru 63-21) and Other Requirements (Reference Number 64-1) are explained and important information to be discussed is identified. Special emphasis is placed on the evaluation of Topics 61-1,2,3 and 62-1,2,3 to assure that the occurance of any especially toxic impurities in a product are examined in detail.

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STANDARD EVALUATION PROCEDURE

PREAMBLE

This Standard Evaluation Procedure (SEP) is one of a set of guidance documents which explain the procedures used to evaluate environmental and human health effects data submitted to the Office of Pesticide Programs. The SEPs are designed to ensure comprehensive and consistent treatment of major scientific topics in these reviews and to provide interpretive policy guidance where appropriate. The Standard Evaluation Procedures will be used in conjunction with the appropriate Pesticide Assessment Guidelines and other Agency Guidelines. While the documents were developed to explain specifically the principles of scientific evaluation within the Office of Pesticide Programs, they may also be used by other offices in the Agency in the evaluation of studies and scientific data. The Standard Evaluation Procedures will also serve as valuable internal reference documents and will inform the public and regulated community of important considerations in the evaluation of test data for determining chemical hazards. I believe the SEPs will improve both the quality of science within EPA and, in conjunction with the Pesticide Assessment Guidelines, will lead to more effective use of both public and private resources.

Anne L. Barton, Acting Director
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PRODUCT CHEMISTRY

I. INTRODUCTION

A. Purpose of the Standard Evaluation Procedure

This procedure is designed to aid Residue Chemistry Branch (RCB) reviewers in their evaluations of studies submitted by manufacturers/registrants/petitioners on the chemistry of their products.

B. Background Information

A product chemistry profile of a pesticide product is required under "Data Requirements for Pesticide Registration; Final Rule" (49 FR (207) 42890, October 24, 1984) (40 CFR 158.190) to support its registration or reregistration.

Certain product chemistry information is also required when petitions for tolerances for pesticides are submitted for review. These data should be contained in Section A of the petition.

C. Objective of Product Chemistry

Product chemistry data should answer the question: What is the chemical nature of the pesticide product for which registration or establishment of tolerances is being considered?

II. INFORMATION TO BE SUPPLIED

The manufacturer's/registrant's/petitioner's reports should include all information necessary to provide complete and accurate topical discussions of the pesticide product: the identity of its active ingredient, impurities and intentionally added ingredients, how it is manufactured, how it may be detected or measured, and how it should be handled and packaged. The latter two requirements do not necessarily pertain to petitions for tolerances.

Pesticide Assessment Guidelines Subdivision D - Product Chemistry - provides guidance for this purpose.

III. THE DATA EVALUATION PROCESS

A. Prepare a Topical Discussion

The reviewer carefully examines and discusses each type of information/data submitted by the manufacturer/registrant/ petitioner. Corresponding to each category of the discussions listed below is the Guidelines Reference Number (See "Data

Requirements for Pesticide Registration; Final Rule," 49 FR (207) 42890, October 24, 1984, which is incorporated herein by this reference) for each of the types of data required under 40 CFR Part 158. These data illustrate the minimum data that the Agency usually requires to adequately assess the chemical characteristics of a pesticide with respect to Registration Standards.

Category of Data	Guidelines Reference Number
Product Identity	61 - 1,2,3
Analysis and Certification of Product Ingredients	62 - 1,2,3
Physical and Chemical Characteristics	63-2 thru 63-21
Other Requirements	64-1

If there is more than one producer of a certain chemical, a complete data set is required for each of the technical products. Exceptions to this would be those physical properties where the material tested would be the purified active ingredient (PAI), i.e., the octanol/water partition coefficient, solubility, vapor pressure, and dissociation constant. The requirement for a complete data set from each producer of a technical chemical would not ordinarily be encountered in a pesticide petition review where only one producer petitions for a tolerance for his technical product.

The following materials may be used to generate product chemistry data: The PAI which is an analytical reference standard chemical; the technical grade active ingredient (TGAI) which is the chemical as it is manufactured before the addition of any inert ingredients; and the manufacturing-use product (MP) which can be the TGAI or the TGAI with inert ingredients added to facilitate the subsequent formulation of the material into the end-use product (EP) which is the chemical in the form in which it is used as a pesticide.

At present, RCB reviews the complete product chemistry data set for the technical product. Data reviewed by RCB for MPs do not include the physical/chemical properties of the MP.

With respect to the product chemistry requirements, it is important to determine that the proper test chemical, i.e., PAI, TGAI, MP, or EP, is employed for each topical requirement in the Product Chemistry Guidelines. This is especially critical with respect to the physical/chemical properties.

Data requirements for pesticide petitions generally include chemical identity, manufacturing process, impurities found in the product and inerts added to the product. A determination of whether added inerts in the product are cleared under appropriate sections of 40 CFR 180.1001 is also required for pesticide petitions (Sections A and/or B).

1. Product Identity (61-1, 61-2, 61-3)

A definition of the pesticide's chemical identity is necessary as the starting point in any review for three reasons: a) to locate relevant scientific literature sources; (b) to determine which pesticide products fall under the regulatory authorities of the Agency; and c) to identify the essential ingredients to be studied in the evaluation of pesticide hazards.

In general, a chemical's identity is defined by names, numbers, and symbols. This can include common names, chemical names, representative trade names, names of manufacturers, molecular formulas and structures, CAS Numbers, Pesticide Chemical Code (Shaughnessy) Numbers, or other alpha/numeric codes.

Beyond this, the identity of the pesticide chemical may need qualification in additional ways. It may include stereoisomers, related compounds, or various complex molecules of indeterminate structure occurring in a mixture. It may also include several derivatives of the pesticide chemical which are known to have similar behavior and effect, as in the case of salts and esters of an acid. An up-to-date description of the manufacturing process of the pesticide chemical and its formulated products is required to probe chemical or biological differences which may be attributable to their manufacture. This description is considered to be Confidential Business Information (CBI), and must be protected. For this reason it is summarized in a confidential appendix.

Information is required on the presence of impurities or contaminants that may result from: a) chemical reactions employed in the synthesis and purification of the active ingredients; b) chemical reactions between the ingredients used in the formulated products; c) chemical reactions between the pesticide ingredients and chemicals that may leach from packing materials; and d) changes in composition of formulated products during storage.

2. Analysis and Certification of Product Ingredients (62-1, 62-2, 62-3)

The submission of analytical methods for the determination of the active ingredients, impurities, and contaminants has a dual purpose: to ascertain that the concentration of active ingredients, impurities, or contaminants

claimed in the labels of any one of the formulated products is correct, and to be used as a regulatory tool in the implementation of enforcement programs carried out by EPA or any other regulatory Agency. The methodology must comply with the Agency's requirements as stated in Part 158 of the CFR and in Guidance Information available from the Agency on individual pesticide chemicals.

This information is not generally required in Section A of a pesticide petition.

3. Physical and Chemical Characteristics (63-2 thru 63-21)

The physical and chemical characteristics of the pesticide chemical are addressed when these are pertinent to: a) the behavior and fate of the pesticide chemical under normal environmental conditions; b) the disclosure of direct/indirect hazard potential during storage, transport, mixing, dilution, and use of the pesticide chemical; and c) reliability of the pesticide chemical used as the experimental source in studies supporting registration submissions other than the one under review. The required characteristics are listed in Part 158 of the CFR.

This information is not generally required in Section A of a pesticide petition.

4. Other Requirements (64-1)

If the Agency requires it, an applicant must submit a sample of the TGAI, the PAI, or formulated product conforming to the limits certified under 62-2.

B. Identify Data Gaps

Using the available guidance, the reviewer looks for data gaps - omissions in the information/data base submitted by the manufacturer/registrant/petitioner in his reports. When applicable and needed for better understanding of the product chemistry, omissions in the information/data are discussed and tabulated. When so identified, they are brought to the attention of the Product Manager/RD and of the manufacturer/registrant/petitioner for corrective action.

If omissions exist in the data submitted, the reviewer must defer judgment until corrective action has been made.

C. Interactions with Other HED Branches

In considering the appropriateness and adequacy of the information/data submitted on product chemistry, the reviewer

must consult with other HED branch(es) on matters which are germane to reaching that decision.

Specific consultations must be made with Toxicology Branch to obtain its opinion on the toxicological significance of the impurities vis-a-vis that of the product originally used in toxicological tests.

Specific referral(s) must be made to the Exposure Assessment Branch to enable it to arrive at its own conclusions regarding the environmental impact of the pesticide product.

APPENDIX 1

MAJOR POINTS TO CONSIDER IN EVALUATING PRODUCT CHEMISTRY

Include the following:

A. Test Compound(s)

- What is the TGAI, and/or MP, and its purity?
- What is the EP(s) and how much of the active ingredient does it contain?
- Does the EP(s) contain any other active ingredient(s)?
- What are the inert ingredients, and are they covered by 40 CFR 180.1001(c) through (e)?
- What is the EPA Registration Number if registered with the Agency?*
- Who produces the active ingredient and where?
- Are there active isomers or related components of the primary active ingredient?
- Is there more than one producer of the chemical? If so, is there a complete data set for each of the technical products?
- Is a complete Product Chemistry data set available for TGAIs and/or MPs?
- Is the proper test chemical being employed for each topical requirement of the Product Chemistry guidelines?

B. Manufacturing Process(es)

- Is the manufacturing process currently in use and adequately described?
- What are the impurities in the starting (beginning) materials?*
- Are the impurities in the starting (beginning) materials likely to contribute to the formation of toxic ingredients?*
- Are deleterious solvents carried over into the product?
- If the active ingredient is produced commercially by two (or more) manufacturing processes, how do the products differ one from the other in their impurities?*
- Is the manufacturing process itself likely to produce toxic ingredients?
- Is all CBI placed in confidential appendices for limited circulation within the Agency?

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*This information is not generally addressed in Section A of a pesticide petition.

C. Certified Limits*

- Has the registrant given routine compositional data and certified his limits?

D. Analytical Methodology*

- Is there a convenient validated method(s) of adequate sensitivity for the active ingredient, impurities and intentionally added ingredients of toxicological concern, in the TGAI, the MP, or EP which is suitable for enforcing their certified limits?

E. Physical/Chemical Properties*

- Are hazards expected from the use or transport of the TGAI, MP, or EP of the active ingredient?
- Is degradation or reaction during storage apt to produce toxic ingredients?

Note (1): Certain ingredients which are generally recognized to be toxic, and which may be anticipated by chemists to be present in the product include (but are not limited to) nitrosamines, dioxins, hexachlorobenzene, and ethylene thiourea.

Note (2): Some physical and chemical properties are not applicable to a given product on the basis of its known chemistry.

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*This information is not generally required in Section A of a pesticide petition.

APPENDIX 2

REVIEWER AIDS MATERIALS

1. Code of Federal Regulations (40 CFR Part 158) General Services Administration, Washington, DC, updated annually.

2. Subdivision D (Product Chemistry) of the Pesticide Assessment Guidelines, prepared by OPTS/EPA, Washington, DC (1982).

3. Acceptable Common Names and Chemical Names for the Ingredient Statement on Pesticide Labels, 4th ed., C.R. Blalock, et al., editors, OPP/EPA (1979) available from National Technical Information Service, Springfield, VA.

4. Farm Chemicals Handbook, Meister Publishing Company, Willoughby, OH, updated annually.

5. Nanogen Index: A Dictionary of Pesticide and Chemical Pollutants, K. Packer, editor, Nanogens International, Freedom, CA, 1975 (updated periodically by supplements).

6. The Pesticide Manual, 7th ed., C.R. Worthing, editor, The British Crop Protection Council, Lavenham Press Limited, Suffolk, England (1983).

7. The Merck Index, 10th ed., M. Windholz, editor, Merck & Company, Inc., Rahway, NJ (1983).

8. Pesticides Manufacturing and Toxic Materials Control Encyclopedia, M. Sittig, Noyes Data Corporation, Park Ridge, NJ (1980).

9. Official Methods of Analysis of the Association of Official Analytical Chemists, 10th-14th eds., W. Horwitz, editor, Association of Official Analytical Chemists, Arlington, VA.

10. Environmental Protection Agency Manual of Chemical Methods for Pesticides and Devices. W.R. Bontoyan, ed., U.S. Environmental Protection Agency. Published and distributed by the Association of Official Analytical Chemists, Arlington, VA (1976).

11. CIPAC Handbook, Vol. 1 (1970) and Vol. 1A (1980) Collaborative Handbook. International Pesticides Analytical Council Limited, Plant Pathology Laboratory, Hatching Green, Harpenden, Hertfordshire, England.

12. Analytical Methods for Pesticides and Plant Growth Regulators. G. Zweig, and J. Sherma, eds. Continuing Series. Academic Press, New York, NY (1963-1978).

13. Dangerous Properties of Industrial Materials, 6th ed., N.I. Sax, Van Nostrand Reinhold Company, New York (1984).

14. American Society for Testing and Materials. Annual Book of ASTM Standards. Continuing Series. American Society for Testing and Materials, 1916 Race Street, Philadelphia, PA 19103.

15. Guidelines for Testing Chemicals, Organization for Economic Cooperation and Development, 1750 Pennsylvania Avenue NW., Washington, DC.

16. Toxic Substances Control - Discussion of premanufacture testing policy and technical issues; Request for comment, Environmental Protection Agency, FEDERAL REGISTER 44 (53) 16240-16292 (March 16, 1979).

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